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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/841,894	04/25/2001	Patricia A. Billing-Medel	6083.US.D2	6734

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Steven F. Weinstock
Abbott Laboratories
Department 377 / AP6D-2
100 Abbott Park Road
Abbott Park, IL 60064-6050

EXAMINER
FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

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Office Action Summary	Application No.	Applicant(s)	
	09/841,894	BILLING-MEDEL ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-16,23-35,38 and 39* is/are pending in the application.

4a) Of the above claim(s) *23-32 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-16,33,35,38 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 18, 2003 has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 10-16, 33, 35, 38 and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that “Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed

by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named SEQ ID Nos 1-16. Thus, applicant has express possession of only these 16 nucleic acids in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided. Further, these claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and only specific amino acid sequences have been provided. No written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at

> 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the SEQ ID Nos 1-16 to comprise the sequence, to claim any 50% identical sequence or to any sequence which hybridizes to the sequence is precisely the situation of naming a type of material which is generally known to likely exist, but, except for the 16 specific sequences, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a PS108 polynucleotide, without any definition of the particular changes due to the % identity, or selectively hybridizing language claimed.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise SEQ ID Nos 1-16. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

1. The rejection under 35 U.S.C. 112, second paragraph, is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 10-16 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Gibco/BRL (1993/1994) p. 7-18.

The Gibco/BRL catalog teaches a kit comprising PUC-19 (see page 7-18). The sequence of PUC 19 is found in Genbank Accession No. M77789 (attached). Below are four alignments of sequence fragments of more than 10 nucleotides which are more than 50% identical to particular claimed SEQ ID NOs. The same result could be obtained with any of the claimed sequences.

PUC 19 is a polynucleotide that is 2686 nucleotides in length (see Genbank record) thereby being larger than 10 nucleotides, which polynucleotide comprises at least one fragment of 16 nucleotides that is 62.5% identical with SEQ ID NO: 1.

```
PUC 19          393 gaggcccgcaccgatc 408
                    ||||||||  |    |
SEQ ID NO 1:    41  gaggcccggagacact 56
```

PUC 19 is a polynucleotide that is 2686 nucleotides in length (see Genbank record) thereby being larger than 10 nucleotides, which polynucleotide comprises at least one fragment of 16 nucleotides that is 75% identical with SEQ ID NO: 2.

```
PUC 19          419 acagttgcgcagcctg 434
                    | | || ||||||||
SEQ ID NO: 2    62  tcggatgggcagcctg 77
```

PUC 19 is a polynucleotide that is 2686 nucleotides in length (see Genbank record) thereby being larger than 10 nucleotides, which polynucleotide comprises at least one fragment of 16 nucleotides that is 68.7% identical with SEQ ID NO: 3.

```
PUC 19          87  gcagtgagcgcaacgc 102
                    ||||||||  || |
SEQ ID NO: 3:   132 gcagtgaggacagcct 147
```

PUC 19 is a polynucleotide that is 2686 nucleotides in length (see Genbank record) thereby being larger than 10 nucleotides, which polynucleotide comprises at least one fragment of 16 nucleotides that is 81.2% identical with SEQ ID NO: 4.

```
PUC 19          930 gcattttgccttcctg 945
                    | ||  ||||||||||
SEQ ID NO: 4    171 ggatagtgccttcctg 186
```

Similar results can be obtained with each of the other claimed SEQ ID Nos.

With regard to claim 12 and 13, the product is identical however it is made. As MPEP 2111.02 notes "Intended use recitations and other types of functional language

cannot be entirely disregarded. However, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." It is clear that a structural difference must exist between the claimed invention and the prior art to overcome the rejection and not simply a difference in the intended use. Here, the mode of synthesis imposes no structural difference on the product.

With regard to claim 14, PUC 19 comprises a variety of different epitopes, since a nucleic acid itself may represent the epitope for antibody binding (see Genbank record).

With regard to claim 15, PUC 19 comprises sequences, as discussed above that comprise open reading frames. Any three nucleotides selected from the sequences shown above represent the open reading frame of a single amino acid. In fact, however, PUC 19 also comprises the open reading frame of the Lac Z enzyme (see Genbank record).

With regard to claim 16, Gibco/BRL catalog expressly teaches transformation of cells with PUC19 (see page 7-18).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 10-16, 33 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guthrie et al (U.S. Patent 5,262,318) in view of Stratagene catalog (1988) p. 39.

Guthrie teaches a cloning procedure in which DNA fragments are run onto DEAE paper and then ligated into PUC19 (see column 16, lines 18-67). As noted above, PUC19 meets the nucleic acid requirement of the claimed invention since it comprises nucleic acids greater than 10 nucleotides which are at least 50% identical to one of SEQ ID Nos: 1-16.

With regard to claim 16, Guthrie teaches transformation of cells with PUC19 (see column 16, lines 49-67).

With regard to claim 35, Guthrie teaches the use of DEAE paper in the cloning procedure (see column 16, lines 18-50).

Guthrie does not teach formation of a kit.

Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Guthrie into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantitites of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantitites you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control" (page 39, column 1). So formation of a kit of Guthrie would be motivated for a number of reasons, including premixing to permit replication and verification of Guthrie's results and minimizing waste in following the Guthrie method.

Response to Arguments

7. Applicant's arguments filed October 2, 2003, 2003 have been fully considered but they are not persuasive.

Applicant argues that the 50% identical language complies with the written description requirement because this determination can be made using prior art references, such as the programs in the Wisconsin group. Applicant argues that this readily available method to determine the nucleic acids encompassed by the claims places the inventors in possession of the claimed invention.

This argument is not found persuasive for two reasons. First, while it is superficially appealing to argue that the percent identity provides structure to the claims, in fact, methods of calculating percent identity vary based upon the algorithm chosen. This algorithm based variation renders the exact set of species encompassed by the genus less certain and the possession less defined. Further, even if a particular algorithm is selected, the genus size for a 258 base pair fragment such as SEQ ID NO: 1 would be immense. The calculation for a single point mutation within this sequence would result in 3 possible substitutions times 258 possible positions. For two changes, the calculation would be (3 x 258) (for the first position) multiplied by (3 x 257) for the second position. Thus, the calculation would be 3^{129} x 258 factorial divided by 129 factorial for 50% possible differences. This is 3.5×10^{61}. Since the number of atoms calculated to be in the universe ranges from 10^{78} to 10^{81}, the number of possible different sequences contained in the genus is very large indeed.

Second, when this immense genus is analyzed in the framework applied by the Federal Circuit in Lilly, Fiers, and Enzo, it is clear that there is no common feature which relates all members of the genus of sequences 50% identical to the specific SEQ ID NO. For example, SEQ ID NO: 6 has 178 nucleotides. These are CTTGGCCAAA

ACTCAGCGT AGAAAACTTC CAGCACATTG GGGTGGAGGG CCTGCCTCAC

TGGGTCCCAG TCCCCGCTC CTGTTAGCCC CATGGGGCTG CCGGGCTGGC

CGCCAGTTTC TGTTGCTGCC AAAGTYATGT GGCTCTCTGC TGCCACCCTG

TGCTGCTGAG GTGCGTANTG CACAGCTGGG GGCTG.

Two members of the claimed genus are

CTTGGCCAAA ACTCAGCGT AGAAAACTTC CAGCACATTG GGGTGGAGGG CCTGCCTCAC TGGGTCCCAG TCCCCGCTC CTGTTAGC and

CC CATGGGGCTG CCGGGCTGGC CGCCAGTTTC TGTTGCTGCC AAAGTYATGT GGCTCTCTGC TGCCACCCTG TGCTGCTGAG GTGCGTANTG CACAGCTGGG GGCTG

Representing the first 88 and the second 88 nucleotides of this sequence. These two sequences are both 50% identical to SEQ ID NO: 6, but share no sequence identity with one another and have no common feature relating them to the genus. Further, without any functional recitation, there is are no necessary common elements which provide informative description of the members of the genus. In Lilly, an insulin sequence with about 80% homology to the prior art and which was functionally limited was found to lack descriptive support. Here, where a lower homology is used and no functional limitations are recited, there is a clear absence of possession of the entire claimed genus.

Lastly, the Written Description guidelines, in example 14, address the issue of percent identity. In that context, two requirements were necessary to comply with the written description requirement. The first was an expectation that the genus would not

substantially vary. In the guidelines, this expectation was met with a 95% identity requirement. Here, with a 50% identity limitation, this expectation is not met. Second, there is a functional requirement of catalytic activity which limits the scope of the genus. In the current claim there are no functional requirements for these nucleic acid sequences and therefore this limitation is not present in the current claim set.

For these reasons, the written description rejection is maintained.

With regard to the prior art rejections, the new amendment necessitated the new rejections.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is currently 703-308-6568. In mid January, 2004, when TC 1600 relocates to the new USPTO facility in Alexandria, the examiner's phone number will become 571-272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The supervisor's new telephone number in mid January will be 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is currently 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman

JEFFREY FREDMAN
PRIMARY EXAMINER